A Programmatic Growth Control Mechanism Comprises an Additional Dynamic Affecting Low-Dose Carcinogenesis Risk

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Imperative in the proper determination of risk of cancer presentation is understanding the mechanisms underlying cancer initiation and progression. Beyond the multi-hit paradigm for cancer initiation and progression due to genetic and epigenetic events, another factor is proposed to be contributory – 'programmed progression' based on awakening of latent embryogenic processes. As there are non-mutagenic origins to cancer, programmatic features may well play a role. One such means may be through recapitulation of organogenic-like control of tissue growth. Utilizing mammographic data from 420 unselected human breast cancers from women declining therapy, we compared tumor growths to the spectrum of growth functions used commonly in population biology. Strikingly, mathematical analysis reveals a self-regulated growth dynamic involving the tumor and its supportive vascular niche that broadly characterizes the tumors examined. Collectively, tumors are seen to grow as if anticipating a final plateau value, dictated initially by the sharp proportional growth of supporting endothelium, followed ultimately by a growth slowdown of the tumor as this ratio rapidly descends to unity. Endothelial governance of tumor growth recapitulates a similar dynamic seen in pancreatic growth, liver growth, and even for bone marrow progenitor cells defining the "pre-metastatic niche". That tumor growth should recapitulate organ development through tumor-endothelial crosstalk suggests the existence of a programmatic growth-control mechanism whose perturbation could also affect final low-dose cancer disease risk, augmenting our mutational understanding of carcinogenesis.

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